Gulf War and Health: Updated Literature Review of Sarin

Testimony of

Samuel Potolicchio, MD
Professor and Clinical Neurologist
The George Washington School of Medicine
Washington, DC

and

Member, Committee on Gulf War and Health: Review of the Medical Literature Relative to Gulf War Veterans Health
and
Member, Committee on Gulf War and Health: Fuels, Combustion Products, and Propellants
and
Member, Committee on Gulf War and Health: Insecticides and Solvents
and
Member, Committee on Gulf War and Health: Depleted Uranium, Pyridostygmine Bromide, Sarin, Vaccines
and
Member, Committee on Gulf War and Health: Update Literature Review of Sarin
Board on Health Promotion and Disease Prevention
Institute of Medicine
The National Academies

before the

Subcommittee on National Security, Emerging Threats, and International Relations
Committee on Government Reform
U.S. House of Representatives

November 15, 2005

Good morning Mr. Chairman and members of the subcommittee. I am Dr. Samuel Potolicchio. I am a clinical neurologist with The George Washington University Hospital. In addition, I have been a volunteer member of the committees that produced or are currently preparing the following four Institute of Medicine (IOM) reports: *Gulf War and Health: Review of the Medical Literature Relative to Gulf War Veterans Health*; *Gulf War and Health: Fuels, Combustion Products, and Propellants*, *Gulf War and Health: Insecticides and Solvents; Gulf War and Health: Depleted Uranium, Pyridostygmine Bromide, Sarin, Vaccines*; and *Gulf War and Health: Updated Literature of Sarin*. Because of my experience on those committees and, in particular, my work on the sarin report, the IOM requested that I testify on the work of the sarin committee. I appreciate this opportunity to speak with you about the sarin report.

The sarin report was conducted following a request from the Department of Veterans Affairs (VA) to update an earlier report on the potential human health effects of sarin. That request followed the publication of a series of toxicology studies in rats looking at the effects of relatively low concentrations of sarin. Sarin is a highly toxic nerve agent produced for chemical warfare. Sarin can be fatal within minutes to hours. It is a member of a class of chemicals known as organophosphorous compounds. In humans and other animals, exposure to high doses of sarin produces a well-characterized syndrome, the acute cholinergic syndrome, featuring a wide variety of signs and symptoms, including: increased salivation, lacrimation (increased tears) and perspiration, "bloody tears", blurring

of vision, nausea, vomiting, diarrhea and fecal incontinence, excessive secretions in the bronchi (respiratory system), tightness in chest, cough, tachycardia (quickened heart rate), increased blood pressure, drowsiness and lethargy, mental confusion, headache, coma and convulsions. It is important to remember that the acute cholinergic syndrome is a very serious effect that requires medical attention and can lead to death.

I would like to note that, as with the committees discussed by Dr. Goldman, at no time during the preparation of *Gulf War and Health: Updated Literature Review of Sarin*, did anyone outside of the committee process influence the work, deliberations or outcomes of the studies.

In drawing its conclusions, the sarin update committee evaluated relevant studies that were identified in searches of databases that identified approximately 250 articles that were potentially relevant to the committee's charge. Those articles included studies in humans and animals. On the basis of those studies the committee reached its conclusions.

The committee, as with previous Gulf War and Health committees, made conclusions regarding the existence of the acute cholinergic syndrome following sarin exposure, the existence of long-term effects in individuals exposed to sarin who had the acute cholinergic syndrome, and the existence of long-terms effects

in individuals exposed to sarin who did not have any signs of having had the acute cholinergic syndrome.

The first conclusion is that there is sufficient evidence of a causal relationship between exposure to sarin and a dose-dependent (effect seen at high doses) acute cholinergic syndrome that is evident seconds to hours after sarin exposure and resolves in days to months. That conclusion is based on data from humans exposed to sarin and is supported by data in animals and on organophosphorous pesticides, which are related chemically to sarin.

The second conclusion is that there is limited/suggestive evidence of an association between exposure to sarin at doses sufficient to cause the acute cholinergic signs and symptoms and a variety of subsequent long-term neurologic effects[1]. As with the previous conclusion, that conclusion is based on data from humans exposed to sarin and is supported by data in animals and data on organophosphorous pesticides.

Finally, the committee concluded that there is inadequate/insufficient evidence of an association between exposure to sarin at low doses insufficient to cause acute cholinergic signs and symptoms and subsequent long-term adverse health effects (specifically, neurologic and cardiovascular effects). That

[1] Many health effects are reported in the literature to persist after sarin exposure: fatigue, headache, visual disturbances (asthenopia, blurred vision, and narrowing of the visual field), asthenia, shoulder stiffness, and symptoms of PTSD. Sarin exposure has been followed by abnormal test results, of unknown clinical

conclusion was based on a lack of data in humans or animals. I will focus on this last conclusion, as the first two conclusions are relatively well established and not controversial.

As with other Gulf War and Health committees, the sarin update committee first reviewed the human studies. There were data from studies of U.S. and U.K. servicemen who several decades ago (1958 through 1984) volunteered to be exposed to chemical weapons, including sarin; industrial workers with documented acute, high-dose exposures to sarin, victims of the sarin terrorist attacks in Japan, and studies of Gulf War veterans. All of those studies, with the exception of the studies of Gulf War veterans, focused on the effects in individuals who had shown the signs and symptoms of the acute cholinergic syndrome and, therefore, do not provide information on the effects of sarin at concentrations below those that cause the acute cholinergic syndrome.

The studies conducted in Gulf War veterans—including U.S., U.K., Danish, and Canadian veterans—were not very useful in making specific conclusions regarding the health effects of sarin because many do not have objective assessments of exposure to sarin (e.g., many rely on self-reports of exposures in surveys taken years after the war or are in individuals not deployed to the Gulf War until after any of the potential exposures to sarin are thought to

---

significance, on the digit symbol test of psychomotor performance, EEG records of sleep, event-related potential, visual evoked potential, and computerized posturography.

have occurred) or have other problems with the exposure assessment. In addition, no health outcomes were consistently seen in those studies.

Given the limitations of the epidemiology studies, the committee then reviewed the available toxicology data, focusing on those studies conducted with doses below those that cause the signs and symptoms of the acute cholinergic syndrome to draw conclusions related to lower exposure to sarin and health effects. Although few studies have evaluated the effects of such doses, a recent series of studies by Dr. Rogene Henderson, which are the studies that prompted the IOM sarin update, have evaluated the effects of low-dose sarin exposure in rats. Those studies did show some alterations in some subtypes of a specific family of receptors in certain areas of the rats' brains, but no consistent and long-term effects were seen in the levels of the neurotransmitters and on behavioral parameters in the rats. The data on receptors indicate further research areas, but are not correlated with any particular health outcome in rats, let alone humans. Those data on receptor density, therefore, are not sufficient to indicate an association with a human health effect, especially given the fact that behavioral effects were not seen in rats treated with sarin at the same concentration. Animal studies by other researchers looking at low-dose effects also showed inconsistent, if any, effects.

In summary, the committee concluded that there is sufficient evidence of a causal relationship between exposure to high amounts of sarin and the acute

cholinergic syndrome and there is limited/suggestive evidence of an association between exposure to sarin at those high levels that cause the acute cholinergic syndrome and a variety of subsequent long-term neurologic effects. However, given the few epidemiology studies, the limitations of those studies that look at the effects of exposure to low concentrations of sarin (i.e., below those that cause the acute cholinergic syndrome), and the limited number of relevant toxicology studies and their inconsistent results, the committee concluded that there was inadequate/insufficient evidence to determine if there is an association between exposure to sarin at levels that do not cause the acute cholinergic syndrome and any human health effects. Those conclusions were based on available scientific data and they were made by the committee without any external pressures or interference.

With that, I would once again like to thank you for inviting me to testify before this subcommittee. I appreciate the work of this Subcommittee on National Security, Emerging Threats, and International Relations and am happy for your interest in this important area of veteran's health. I look forward to answering any questions you might have.